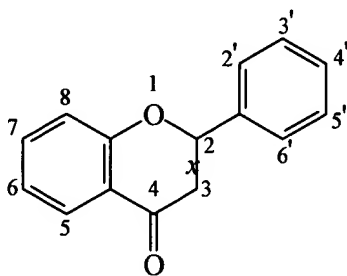


Claims

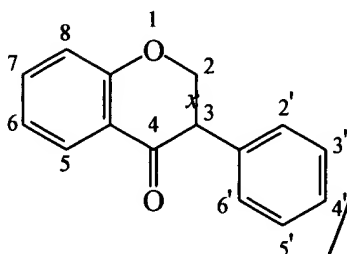
1. A method for enhancing chloride transport in epithelial cells, comprising contacting epithelial cells with a compound selected from the group consisting of flavones and isoflavones, wherein the compound is capable of stimulating chloride transport, and wherein the compound is not genistein.

2. A method according to claim 1, wherein the compound is:

(a) a polyphenolic compound having the general formula:



or



wherein carbon atoms at positions 2, 3, 5, 6, 7, 8, 2', 3', 4', 5' and 6' are bonded to a moiety independently selected from the group consisting of hydrogen atoms, hydroxyl groups and methoxyl groups, and wherein X is a single bond or a double bond;
or

(b) a stereoisomer or glycoside derivative of any of the foregoing polyphenolic compounds.

3. A method according to claim 1, wherein the compound is selected from the group consisting of quercetin, apigenin, kaempferol, biochanin A, flavanone,

flavone, dihydroxyflavone, trimethoxy-apigenin, apigenin 7-O-neohesperidoside, fisetin, rutin, daidzein and prunetin.

4. A method for enhancing chloride transport in epithelial cells, comprising contacting epithelial cells with a compound selected from the group consisting of resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid.

5. A method according to claim 1 or claim 4, wherein the epithelial cells are airway epithelial cells.

6. A method according to claim 5, wherein the airway epithelial cells are present in a mammal.

7. A method according to claim 6, wherein the compound is administered orally.

8. A method according to claim 6, wherein the compound is administered by inhalation.

9. A method according to claim 1 or claim 4, wherein the epithelial cells are intestinal cells.

10. A method according to claim 9, wherein the intestinal epithelial cells are present in a mammal.

11. A method according to claim 10, wherein the compound is administered orally.

12. A method according to claim 1 or claim 4, wherein the epithelial cells are pancreas, gallbladder, sweat duct, salivary gland or mammary epithelial cells.

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13. A method according to claim 12, wherein the intestinal epithelial cells are present in a mammal.

14. A method according to claim 1 or claim 4, wherein the cells are further contacted with a substance that increases (a) trafficking of a CFTR to the plasma membrane of the cells; and/or (b) expression of a CFTR in the cells.

15. A method according to claim 1 or claim 4, wherein the compound is present within a pharmaceutical composition comprising a physiologically acceptable carrier or excipient.

16. A method according to claim 1 or claim 4, wherein the epithelial cells produce a mutated CFTR protein.

17. A method according to claim 16, wherein the mutated CFTR protein has a deletion at position 508 or a point mutation at position 551.

18. A method according to claim 1 or claim 4, wherein the pharmaceutical composition further comprises a substance that increases (a) trafficking of a CFTR to the plasma membrane of the cells; and/or (b) expression of a CFTR in the cells.

19. A method according to claim 18, wherein the substance increases expression of a CFTR in the cells and is 4-phenylbutyrate or sodium butyrate.

20. A method according to claim 18, wherein the substance is a chemical chaperone that increases trafficking of a CFTR to the plasma membrane of the cells, and wherein the compound is selected from the group consisting of glycerol, dimethylsulfoxide, trimethylamine N-oxide, taurin, methylamine and deoxyspergualin.

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21. A method according to claim 1, wherein the cells are further contacted with a compound selected from the group consisting of resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid.

22. A method according to claim 21, wherein the cells are contacted with a polyphenolic compound and ascorbic acid.

23. A method according to claim 22, wherein the polyphenolic compound is genistein, daidzein or prunetin.

24. A method for enhancing chloride transport in epithelial cells, comprising contacting epithelial cells with genistein, wherein the epithelial cells produce a mutated CFTR protein.

25. A method according to claim 24, wherein the mutated CFTR protein is G551D-CFTR or $\Delta F508$ -CFTR.

26. A method according to claim 24, wherein the epithelial cells are further contacted with a substance that increases (a) trafficking of a CFTR to the plasma membrane of the cells; and/or (b) expression of a CFTR in the cells.

27. A method according to claim 26, wherein the substance increases expression of a CFTR in the cells and is 4-phenylbutyrate or sodium butyrate.

28. A method according to claim 26, wherein the substance is a chemical chaperone that increases trafficking of a CFTR to the plasma membrane of the cells, and wherein the compound is selected from the group consisting of glycerol, dimethylsulfoxide, trimethylamine N-oxide, taurin, methylamine and deoxyspergualin.

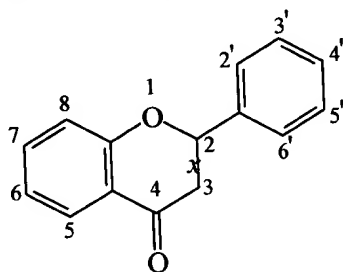
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29. A method for enhancing chloride transport in epithelial cells, comprising contacting epithelial cells with genistein and a compound selected from the group consisting of resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid.

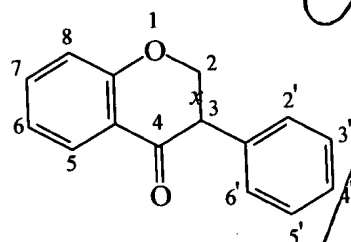
30. A method for treating cystic fibrosis in a mammal, comprising administering to a mammal one or more compounds selected from the group consisting of flavones and isoflavones, wherein the compound is capable of stimulating chloride secretion, and thereby treating cystic fibrosis in the mammal.

31. A method according to claim 30, wherein the compound is:

(a) a polyphenolic compound having the general formula:



or



wherein carbon atoms at positions 2, 3, 5, 6, 7, 8, 2', 3', 4', 5' and 6' are bonded to a moiety independently selected from the group consisting of hydrogen atoms, hydroxyl groups and methoxyl groups, and wherein X is a single bond or a double bond;

or

(b) a stereoisomer or glycoside derivative of any of the foregoing polyphenolic compounds.

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32. A method according to claim 31, wherein the compound is selected from the group consisting of quercetin, apigenin, kaempferol, biochanin A, flavanone, flavone, dihydroxyflavone, trimethoxy-apigenin, apigenin 7-O-neohesperidoside, fisetin, rutin, daidzein and prunetin.

33. A method according to claim 31, wherein the compound is genistein.

34. A method for treating cystic fibrosis in a mammal, comprising administering to a mammal one or more compounds selected from the group consisting of resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid.

35. A method according to claim 30 or claim 34, wherein the compound is administered orally.

36. A method according to ~~claim~~ 30 or claim 34, wherein the compound is administered by inhalation.

37. A method according to claim 30 or claim 34, wherein a substance is further administered to the mammal, such that the substance increases (a) trafficking of a CFTR to the plasma membrane of epithelial cells; and/or (b) expression of a CFTR in epithelial cells.

38. A method according to claim 37, wherein the substance increases expression of a CFTR in the cells and is 4-phenylbutyrate or sodium butyrate.

39. A method according to claim 37, wherein the substance is a chemical chaperone that increases trafficking of a CFTR to the plasma membrane of the cells, and wherein the compound is selected from the group consisting of glycerol, dimethylsulfoxide, trimethylamine N-oxide, taurin, methylamine and deoxyspergualin.

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40. A method according to claim 30, wherein the compound is present within a pharmaceutical composition comprising a physiologically acceptable carrier or excipient.

41. A method according to claim 40, wherein the pharmaceutical composition further comprises a compound selected from the group consisting of resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid.

42. A method according to claim 40, wherein the pharmaceutical composition further comprises a substance that increases (a) trafficking of a CFTR to the plasma membrane of epithelial cells; and/or (b) expression of a CFTR in epithelial cells.

43. A method according to claim 40, wherein the substance increases expression of a CFTR in the cells and is 4-phenylbutyrate or sodium butyrate.

44. A method according to claim 42, wherein the substance is a chemical chaperone that increases trafficking of a CFTR to the plasma membrane of the cells, and wherein the compound is selected from the group consisting of glycerol, dimethylsulfoxide, trimethylamine N-oxide, taurin, methylamine and deoxyspergualin.

45. A method for increasing chloride ion conductance in airway epithelial cells of a patient afflicted with cystic fibrosis, wherein the patient's CFTR protein has a deletion at position 508, the method comprising administering to a mammal one or more compounds selected from the group consisting of flavones and isoflavones, wherein the compound is capable of stimulating chloride secretion.

46. A method according to claim 45, wherein the compound is genistein.

47. A method according to claim 45, wherein the compound is quercetin.

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48. A method for increasing chloride ion conductance in airway epithelial cells of a patient afflicted with cystic fibrosis, wherein the patient's CFTR protein has a mutation at position 551, the method comprising administering to a mammal one or more compounds selected from the group consisting of flavones and isoflavones, wherein the compound is capable of stimulating chloride secretion.

49. A method according to claim 48, wherein the compound is genistein.

50. A method according to claim 48, wherein the compound is quercetin.

51. A pharmaceutical composition for treatment of cystic fibrosis, comprising:

(a) one or more flavones or isoflavones capable of stimulating chloride secretion;

(b) one or more of:

(i) a compound that increases expression of a CFTR in an epithelial cell; and/or

(ii) a chemical chaperone that increases trafficking of a CFTR to a plasma membrane in an epithelial cell; and

(c) a physiologically acceptable carrier.

52. A pharmaceutical composition for treatment of cystic fibrosis, comprising:

(a) genistein;

(b) one or more of:

(i) a compound that increases expression of a CFTR in an epithelial cell; and/or

FOOTNOTES

(ii) a chemical chaperone that increases trafficking of a CFTR to a plasma membrane in an epithelial cell; and

(c) a physiologically acceptable carrier.

53. A pharmaceutical composition for treatment of cystic fibrosis, comprising:

(a) quercetin;

(b) one or more of:

(i) a compound that increases expression of a CFTR in an epithelial cell; and/or

(ii) a chemical chaperone that increases trafficking of a CFTR to a plasma membrane in an epithelial cell; and

(c) a physiologically acceptable carrier.

54. A pharmaceutical composition for treatment of cystic fibrosis, comprising:

(a) apigenin;

(b) one or more of:

(i) a compound that increases expression of a CFTR in an epithelial cell; and/or

(ii) a chemical chaperone that increases trafficking of a CFTR to a plasma membrane in an epithelial cell; and

(c) a physiologically acceptable carrier.

55. A pharmaceutical composition for treatment of cystic fibrosis, comprising:

(a) kaempferol;

(b) one or more of:

(i) a compound that increases expression of a CFTR in an epithelial cell; and/or

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- (c) a physiologically acceptable carrier.

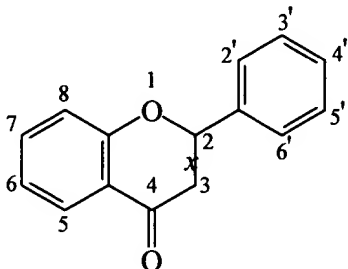
(a) biochanin A;

(b) one or more of:

(ii) a chemical chaperone that increases trafficking of a CFTR to the apical surface of an epithelial cell; and

(c) a physiologically acceptable carrier.

(a) a polyphenolic compound having the general formula:



Chemical structure of 2-phenyl-4H-pyran-4-one. The pyran ring is numbered 1-8, and the phenyl ring is numbered 1'-6'.

wherein carbon atoms at positions 2, 3, 5, 6, 7, 8, 2', 3', 4', 5' and 6' are bonded to a moiety independently selected from the group consisting of hydrogen atoms,

(c) a physiologically acceptable carrier.

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